IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of	:	Ralph L. Bass	Confirmation No.: 2281
Docket No.	:	014123-000008	
Application No.	:	09/721,131	
Art Unit	:	1616	
Filed	:	November 22, 2000	
Examiner	:	Frank Choi	
Title	:	METHOD FOR TREATING HIV	

Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

RESPONSE TO OFFICIAL ACTION

Sir:

This is responsive to the Official Action dated June 18, 2003, having a 3-month, statutory term that expired on September 18, 2003. A Petition for a 3-month extension of time, up to and including December 18, 2003 is enclosed, together with a $475.00 check (small entity status) for the requisite fee for the extension.

Favorable reconsideration is respectfully requested in view of the following.

REMARKS

Issues.

The main issues are whether applicant has adequately enabled his invention and whether his invention has credible utility, when applicant's specification has specific detailed prophetic Laboratory Examples, but no actual working Laboratory Examples, for applicant's inventive method of treating a human having HIV with sodium chloride (afterwards referred to by its chemical symbol, NaCl).

Summary of selected claims.

Claim 22. The present invention, as defined in this claim (the only independent claim), is directed to administering a NaCl formulation to an HIV-infected person, where the amount of NaCl is more than the person's average daily intake but less than the toxic amount (defined as

measured by TCLo and as measured by LD50), and periodically repeating the administration, thereby achieving alleviation of the HIV infection.

Claim 28. The present invention, as defined in this dependent claim (which has dependency going back to independent claim 22) is directed to the mixture of NaCl and potassium containing another ingredient selected from sulfur, phosphorus, zinc, manganese, iron, copper, chromium, iodine, magnesium, cobalt, selenium, or combinations thereof.

Claim 35. The present invention, as defined in this dependent claim (which has dependency going back to independent claim 22) is directed to various types of administration of a solid formulation of the NaCl, namely oral, sublingual, buccal, transdermal, or a combination thereof.

Discussion of rejection of claims 22 - 42 under 35 U.S.C. §101 for lack of credible utility and under 35 U.S.C. §112, first paragraph, for lack of enablement.

Sodium chloride, potassium, sulfur, phosphorus, zinc, manganese, iron, copper, chromium, iodine, magnesium, cobalt, and selenium, *are all nutrients required by the human body*. Each of these nutrients is recited in one or more of applicant's claims.

In the present Official Action, the Examiner has reiterated that the specification does not appear to show any working examples, but appears to provide only hypothetical statements of what would occur.

Moreover, the Examiner now cites *Ex parte Sudilovsky*, 21 USPQ2d 1702, 1705 (Bd Pat Appl & Int 1991) for the proposition that although lack of working examples is not controlling in determining whether a disclosure meets the enablement requirement of 35 U.S.C. §112, when a patent applicant chooses to forego exemplification and bases utility on broad terminology and general allegations, he runs the risk that unless one with ordinary skill in the art would accept the allegations as obviously valid and correct, the Examiner may, properly, ask for evidence to substantiate them.

With regard to enablement under 35 U.S.C. §112, first paragraph, applicant respectfully points out that he did <u>not</u> base utility on broad terminology and general allegations, in contrast to Sudilovsky.

Rather, applicant's prophetic Laboratory Examples and specification teach in great detail periodic administration of a certain amount of NaCl (more than the person's average daily intake, but less than the toxic amount which would kill the person, i.e., less than the amount of NaCl as measured by TCLo and as measured by LD50) to an HIV-infected person in order to alleviate the HIV infection. The Laboratory Examples are very detailed and specific about determining the average daily intake and the amounts and frequency of NaCl to be administered to the person.

On the other hand, Sudilovsky's application merely had broad terminology and general allegations of a "treatment effective amount" of the angiotensin converting enzyme inhibitor alone or in combination with a calcium channel blocker. There are no details on the amounts and frequency of the angiotensin converting enzyme inhibitor to be administered to the person.

Furthermore, the Examiner has now stated in the present Official Action that:

> Arguments of counsel alone cannot take the place of evidence in the record once an examiner has advanced a reasonable basis for questioning the disclosure. See In re Budnick, 190 USPQ at 424; In re Schulze, 145 USPQ 716 (CCPA 1965); In re Cole, 140 USPQ 230 (CCPA 1964). For example, in a case where the record consisted substantially of arguments and opinions of applicant's attorney, the court indicated that factual affidavits could have provided important evidence on the issue of enablement. See In re Knowlton, 183 USPQ at 37; In re Wiseman, 201 USPQ 658 (CCPA 1979).

Contrary to the Examiner's allegations, the Examiner has **not** advanced a reasonable basis for questioning the disclosure and the record does **not** consist substantially of arguments and opinions of applicant's attorney.

Rather, as stated above, applicant's prophetic Laboratory Examples are very detailed and specific about determining the average daily intake and the amounts and frequency of NaCl to be administered to the person.

Thus, applicant's specification and prophetic Laboratory Examples are clearly sufficient to teach the person of ordinary skill in the art how to make and to use the invention, without undue experimentation. And that is why the Examiner is clearly erroneous in now reinstating his rejection of all of the claims that he had made in the first Official Action for lack of enablement under 35 U.S.C. §112, first paragraph.

Additionally, the Examiner has noted that applicant's argued but not disclosed mechanism by which administration of NaCl results in reduction of HIV infection appears to be unsupported by evidence showing that the disclosed effective levels of NaCl would be sufficient to alleviate HIV.

As previously stated, *although applicant does not intend to be bound to any theory, he believes the following describes the how and the why, i.e., the mechanism, of his invention.*

As is well known to those of ordinary skill in the art, HIV virus cells are small as compared to large human cells, which is discussed in the Merck brochure entitled "Livin'It", that applicant forwarded to the Examiner. Specifically, a drawing on the first two pages shows the smaller HIV virus cell in red attached to the larger human CD4 T-cell in blue, and is followed by a discussion of how an HIV infection occurs. The HIV virus cell does not have DNA but rather has only viral RNA and thus cannot replicate on its own. Instead, the HIV virus cell replicates by using the DNA of the human CD4 T-cell to which the HIV virus cell is attached.

Applicant in previous responses has presented his *theory* that how and why his invention works is that periodic administration of NaCl beyond the average daily intake, but less than the toxic amount, should not disrupt the larger human cells, but should be enough to disrupt the smaller HIV virus cells by changing osmotic pressure enough to dehydrate the smaller HIV virus cells so they should rupture. Since the particular amount of NaCl is still less than the toxic amount, the osmotic pressure should not be changed enough to dehydrate the larger human body cells so they should not rupture. Thus, the disruption/rupturing of the smaller HIV virus cells should cause them to be removed from the larger human cells, and alleviate the HIV infection.

Also, the Examiner has stated in the present Official Action that applicant indicates administration of NaCl should result in circulating levels of NaCl within the range of about 0.05 μM to about 1.0 μM and that the extra amount of NaCl "will" disrupt the HIV virus.

Applicant did not state that the extra amount "will" disrupt the HIV virus. Rather, applicant stated applicant "theorizes" that the extra amount will disrupt the HIV. The disruption is only applicant's theory of the mechanism of his invention.

In connection with this, the Examiner once again has noted that in US Patent No. 5,661,023 to Hrinda et al., it is disclosed that NaCl concentrations as high as 1.4 M for prolonged periods, such as greater than 18 hours, only resulted in partial disassembling of HIV particles. Particularly with respect to Hrinda et al., the Examiner stated that "Applicant has not provided

sufficient and credible evidence showing that the washing of HIV from TMAE FRACTOGEL® resin in a column with sodium chloride solution correlates to alleviation of HIV infection."

Applicant respectfully submits that it is the Examiner who has not correlated Hrinda et al. to applicant's invention and who is quoting applicant out of context.

What applicant stated regarding Hrinda et al. is that they increased the concentration of NaCl in phosphate buffered saline (PBS) to remove HIV cells from TMAE FRACTOGEL® resin, and applicant theorizes that increasing the amount of NaCl more than the HIV-infected person's average daily intake for periodic administration will remove HIV cells from human CD4 T-cells. Thus, one could also argue in the alternative that the person of ordinary skill in the art would expect the claimed invention to function as is clearly illustrated by the prophetic examples and the specification because that skilled artisan would be aware of how HIV infects a person (for instance, the explanation in the Merck brochure) and as a result, would expect HIV particles attached to human CD4 T-cells to behave like and be removed like the Hrinda et al. disclosure of HIV particles from TMAE FRACTOGEL® resin by increasing the NaCl concentration in the PBS.

Applicant respectfully points out, as discussed in more detail below, that the Examiner has committed a fallacious type of argument as the Examiner has left out of his comments vis-à-vis disruption of HIV cells that the levels of NaCl shown by Hrinda et al. are for HIV cells in PBS, not for HIV cells in the human body. As the Examiner should be well aware, it is impermissible to ignore parts of a reference. As stated before, applicant's circulating levels of about 0.05 μM to about 1.0 μM NaCl shown by applicant for his preferred embodiment are from periodic administration of NaCl to a human in an amount more than the person's average daily intake for attacking HIV cells attached to CD4 T-cells in the human body.

Applicant respectfully reiterates that the Examiner is ignoring the details of the Hrinda et al. elution process for obtaining HIV particles, which applicant once more summarizes as follows.

Hrinda et al. inactivate HIV particles by beta-propriolactone (BPL) for about 18 – 24 hours, followed by flowing the BPL-treated HIV particles through a membrane to concentrate them. They are then buffered with phosphate buffered saline (PBS) and passed through columns filled with an anion exchange resin, such as TMAE FRACTOGEL®.

The HIV particles attach to the resin and are subsequently washed with 0.1 - 0.55 M NaCl, buffered at a pH of 6 - 7.5. The attached HIV particles are eluted off the resin using a higher NaCl concentration at 0.6 - 2 M, preferably 0.8 - 1.4 M, at the same buffered pH of 6 - 7.5.

Then, the eluant containing the retroviral particles, particularly HIV, is diluted to reduce the NaCl concentration to within the range of 0.05 - 0.25 M. Hrinda et al. state that this is to prevent the partial disassembling of the HIV-1 particles when exposed to the eluant's high NaCl concentration for prolonged periods of time, such as greater than 18 hours.

Thus, the NaCl concentrations noted by the Examiner, namely "concentrations as high as 1.4 M for prolonged periods, such as greater than 18 hours" that Hrinda et al. use in order avoid partially disassembling HIV particles, are concentrations for HIV particles floating in PBS.

In contrast, applicant's desirable circulating levels of NaCl within a range of about 0.05 μM to about 1.0 μM, as set out at lines 11 and 12 of page 12 of his specification, are concentrations in human blood in a human body for HIV particles attached to human CD4 T-cells from periodic administration of NaCl to a human in an amount more than the person's average daily intake, not for HIV particles floating in PBS.

Applicant respectfully reiterates that the person of ordinary skill in the art will know that PBS is not coursing through the veins and arteries of the human body, nor are HIV cells free floating in the human body. Furthermore, that person will be aware of how HIV infects a person (for instance, the explanation in the Merck brochure).

As a result, the person of ordinary skill in the art would expect that HIV cells attached to CD4 T-cells in the human body should act differently from free HIV cells floating in PBS.

Accordingly, the person of ordinary skill in the art would expect the claimed invention to function as a treatment for HIV infection in a human, as is clearly illustrated by the prophetic examples and the specification. The skilled artisan would not expect HIV particles attached to human CD4 T-cells to behave like the Hrinda et al. disclosure of HIV particles free floating in PBS.

Nevertheless, it does not matter how Hrinda et al. remove the HIV from the resin or how they treat the HIV free floating in PBS because NaCl disrupting small HIV cells to remove them from larger human cells is only applicant's theory of how his invention works. Applicant has no claims requiring that this theorized mechanism is in fact how his invention works.

Also, applicant once more respectfully reiterates the distinction between an enablement issue under 35 U.S.C. §112, first paragraph, and a credible utility issue under 35 U.S.C. §101, with respect to an application having prophetic examples instead of working examples, as follows.

1. There is no legal requirement for actual working examples; therefore, prophetic examples are acceptable. The reason is that the filing of an application constitutes a constructive reduction to practice of the invention. See, *Atlas Powder Co. v. E.I. Du Pont De Nemours & Co.*, 224 U.S.P.Q. 409 (Fed. Cir. 1984).

2. There is no legal requirement for an inventor to set forth correctly, or even to know, how or why the invention works. See, *In Re Cortright*, 49 U.S.P.Q.2d 1464, 165 F.3d 1353 (Fed. Cir. 1999).

Cortright's application matured into her U.S. Patent No. 6,033,676, which involved rubbing 8-hydroxy-quinoline sulfate, the active agent in Bag Balm®, into the scalp to treat baldness. The application had no laboratory data, either prophetic or actual, showing that the effects of lower male hormone levels had been offset by Bag Balm® which had reached the papilla, as required by the language in claim 15. Moreover, the "GENERAL" section at the end of her specification (see, line 50 of column 2 of U.S. Patent No. 6,033,676) started with "Applicant surmises..." prefacing the discussion of offsetting lower male hormone levels by reaching the papilla. Hence, her specification clearly set out that this mechanism was only a theory, not a teaching of how to use.

However, Cortright's claim 15 set out as requirements her **surmised theory** and required offsetting the effects of lower levels of a male hormone being supplied by arteries to the papilla of scalp hair follicles with the active agent 8-hydroxy-quinoline sulfate, to cause hair to grow again on the scalp, by rubbing into the scalp the ointment having the active agent 8-hydroxy-quinoline sulfate 0.3 % carried in a petrolatum and lanolin base so that the active agent reaches the papilla.

The Court of Appeals specifically stated that it is not a requirement of patentability that an inventor correctly set forth, or even know, how or why the invention works. Thus, Cortright

was not required to prove the cause of the hair growth, and claim 15 was not invalid for lack of utility under 35 U.S.C. §101. However, claim 15 was invalid for not satisfying the how to use requirement of 35 U.S.C. §112, first paragraph.

In contrast, the present claims do **not** set out as claim requirements applicant's **surmised theory** of how to use his invention by the periodic administration of the extra amount of NaCl beyond the average daily intake disrupting the relatively smaller HIV cell, and removing it from the relatively larger human cell. Thus, there is no need for working examples, nor anything else, for applicant to prove how his invention works.

The Examiner also reiterated his belief that a method of alleviating HIV infection by administration of NaCl is inherently suspect.

Applicant respectfully reiterates out that treating HIV infection was once considered an inherently unbelievable undertaking, but since then, treatments for HIV infection have gained acceptance, and both AZT (zidovudine) and 3TC (lamivudine) are recognized as effective for treating HIV infection. Similarly, the Court of Appeals in *In Re Cortright, supra* noted that treating baldness was once considered an inherently unbelievable undertaking, but since then, treatments for baldness have gained acceptance, and ROGAINE® (minoxidil) and PROPECIA® (finasteride) are recognized as effective for treating baldness.

Applicant comments as follows on the 38 references submitted, namely copies of Abstracts of 38 research studies (mostly in vivo studies for HIV-infected persons and a few in vitro studies) as published in various journals. These 38 references are listed by the Examiner in the present Official Action.

The Examiner noted that the issues of utility and enablement must be determined as of the November 22, 2000 filing date of the application, but some of the 38 references were published after this date. The references published after this date are numbers 1 - 6, and 10 – 19, and so applicant withdraws them.

The remaining research studies 7 – 9 and 20 – 38 have reported a correlation between a decrease in the ability of HIV-infected persons to inhibit HIV and the presence in these HIV-infected persons of a deficiency for various nutrients, such as sulfur, phosphorus, zinc, manganese, iron, copper, chromium, iodine, magnesium, cobalt, and selenium.

The Examiner noted these references do not disclose a causal correlation between the nutrient and alleviation of HIV infection.

However, applicant respectfully points out that the issue does not rest on these references failing to show nutritional supplementation causes HIV to be inhibited, but rather the issue rests on these references showing a correlation that suggests to the person of ordinary skill that it is credible that supplementation of nutrients could play a role in treatment of HIV.

The Examiner is correct that the research studies do not address the nutrients, sodium chloride and potassium. If the references did, then they would anticipate applicant's claimed invention.

Applicant respectfully submits that the person of ordinary skill in the art would know that sodium chloride is a nutrient and so are potassium, sulfur, phosphorus, zinc, manganese, iron, copper, chromium, iodine, magnesium, cobalt, and selenium. Also, the person of ordinary skill in the art would be aware of many, if not all, of these research studies. Thus, on the basis of those research studies, the person of ordinary skill in the art would conclude credible utility exists for applicant's invention.

Accordingly, applicant respectfully requests the Examiner to withdraw the rejection of claims 22 - 42 under §101 and under §112, first paragraph.

Discussion of separate patentability for dependent claim 28, which is included in the Examiner's rejection of claims 22 - 42 under 35 U.S.C. §101 for lack of credible utility and under 35 U.S.C. §112, first paragraph, for lack of enablement.

With respect to the Examiner's discussion of the 38 references in the present Official Action, the Examiner repeatedly made statements such as "no claim requires the presence of zinc", "no claim requires the presence of selenium", and "no claim requires the presence of zinc, copper or magnesium".

Applicant respectfully points out that each of zinc, selenium, copper, and magnesium is indeed recited in applicant's claim 28.

Thus, the comments above vis-à-vis enablement and credible utility are reincorporated here by reference specifically with regard to claim 28.

Hence, one of ordinary skill in the art would conclude that applicant's invention as per dependent claim 28 for having the mixture of NaCl and potassium that is periodically administered to an HIV-infected person contain nutrients chosen from sulfur, phosphorus, zinc, manganese, iron, copper, chromium, iodine, magnesium, cobalt, and/or selenium would be

credible for treatment of HIV, and enabled by the application. Thus, that person would conclude that credible utility and enablement are most certainly present for dependent claim 28.

Accordingly, applicant respectfully requests the Examiner to withdraw the rejection of claim 28 under §101 and under §112, first paragraph.

Discussion of rejection of claim 35 under §112, first paragraph, for the specification not enabling transdermal administration.

The Examiner reiterated in the present Official Action his rejection of claim 35 under the first paragraph of §112 for no enablement of transdermal administration.

Applicant respectfully reiterates that, as well known to the person of ordinary skill in the art, transdermal administration is effected with a skin patch containing various chemicals, in addition to the agent that it is desired to administer transdermally. Skin patches for transdermal administration of various agents are well known, and applicant is not claiming to have invented transdermal skin patches.

Since skin patches are widely used for administration of various medicaments, the person of ordinary skill in the art of skin patches knows how to make them, without undue experimentation, absent any teaching from applicant's specification. Moreover, applicant clearly provided enablement by the reference on lines 13 - 15 of page 5 of his specification vis-a-vis an explanation of transdermal administration being in US Patent No. 5,016,652.

Therefore, applicant respectfully requests the Examiner to withdraw the rejection of claim 35 under the first paragraph of §112.

CONCLUSIONS

Applicant respectfully submits that the present invention as claimed is enabled by the specification in such a way as to convey to the person of ordinary skill in the art that applicant had possession of the claimed invention and in such a way as to teach a person of ordinary skill in the art how to make and/or how to use the invention without undue experimentation. The filing of the application with prophetic Laboratory Examples is a constructive reduction to practice. Furthermore, applicant, unlike Sudilovsky, did not employ broad terminology and

general allegations. Accordingly, the Examiner is respectfully requested to withdraw his rejection of claims 22 - 44 under §112, for lack of enablement due to the lack of working examples.

Moreover, applicant respectfully submits that the present invention as claimed has credible utility, as there is no requirement that an inventor set forth, or know how or why the invention works. Thus, applicant respectfully requests the Examiner to withdraw the rejection of claims 22 - 44 under §101.

Also, applicant respectfully submits that transdermal administration not only is clearly enabled by applicant's specification, but also is well known to the person of ordinary skill in the art. Hence, applicant respectfully requests the Examiner to withdraw the rejection of claim 35 under the first paragraph of §112.

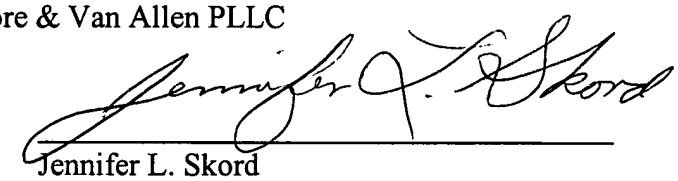
Applicant respectfully submits that the present application is in proper condition for allowance and respectfully requests the Examiner to issue official notification of allowance.

DEPOSIT ACCOUNT

Although a check in the amount of $475.00 is enclosed for the fee for the 3- month extension, and it is believed that no further fee is due, the Commissioner is hereby authorized to charge any deficiencies of payment associated with this Communication, or to credit any overpayment, to Deposit Account No. 13-4365.

Respectfully submitted,

Moore & Van Allen PLLC

Date: December 17, 2003 By: 

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Enclosures: Petition for 3-month extension
Check in the amount of $475.00 (small entity) for fee for 3-month extension

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Filed:	November 22, 2000	Examiner:	Frank Choi
For:	Method for Treating HIV	Confirmation No.:	2281

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Katie Efland
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Date: December 17, 2003